REMARKS

I. Status of claims

Claim 1, 6, and 36 are amended.

Claim 2 is cancelled.

Claims 3-5, 7-35 and 37 are withdrawn.

Claims 1, 6, and 36 are pending.

II. Claims are Enabled

Claims 1, 2, 6, and 36 were rejected under 35 U.S.C. 112, first paragraph based on arguments that cancer treatment was not enabled.

The examiner admitted the claims are enabled "in vitro," e.g., in cultivated cells.

> Gadd 45ß binds to and inhibits JNKK2, thereby down regulating the JNK pathway *in vitro* (par. 00072).

(Office Action mailed March 30, 2006, page 6)

and that

> none of the claims are drawn specifically to the treatment of cancer.

(Office Action mailed November 29, 2006, page 3)

Enablement is satisfied by showing the invention works for its **stated effects in a model** accepted in the art. The effects claimed are blocking suppression of activation of JNK thereby leading to increased cell death. The *in vitro* models used are standard and have been shown to reasonably correlate to *in vivo* effects. Despite shortcomings which characterize all models, which is why they are "models" only, showing the claimed effects is sufficient to proceed to further *in vivo* trials, which requires patent protection for the claimed steps. Biochemical pathways in models of cultivated cells are well accepted in the art, even if there are uncertainties in the entire organism and biochemical effects of the JNK pathway were demonstrated in well established models of cultivated cells.

Apoptosis is the active participation of the cell in its own destruction through the execution of an intrinsic suicide program. Some of the factors in apoptosis have been studies by those of skill in the art using knock-out models, such as that used in the inventors' declaration.

The MPEP states the following at MPEP 2164.02:

> "Correlation" as used herein refers to the relationship between in vitro or in vivo animal model assays and a disclosed or a claimed method of use. An in vitro or in vivo animal model example in the specification, in effect, constitutes a "working example" if that example "correlates" with a disclosed or claimed method invention. If there is no correlation, then the examples do not constitute "working examples." In this regard, the issue of "correlation" is also dependent on the state of the prior art. In other words, if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate. .... *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (reversing the PTO decision based on finding that in vitro data did not support in vivo applications). (*emphasis added*).
>
> Since the initial burden is on the examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of lack of correlation for an in vitro or in vivo animal model example. A rigorous or an invariable exact correlation is not required, as stated in *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985):
>
> > [B]ased upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed in vitro utility and an in vivo activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence. (Citations omitted.) (emphasis added)

Furthermore, the examiner acknowledges that the *in vivo* data presented in the inventor's declaration:

> shows physiological effects of complete Gadd 45ß gene knock out.

(Office Action mailed November 29, 2006, page 3).

The specification also provides data showing that a cell permeable peptide having a peptide sequence derived from JNKK2-Gadd45β binding region binds to Gadd45β and thereby prevents the Gadd45β-dependent inhibition of JNKK2. Thus, the cell-permeable peptide, e.g., peptide GPVWKMRFRKTGHVIAVKQMRRSGN (designated as Peptide 1) relieves the JNKK2 suppression by Gadd45β. In other words, Gadd45β present in the cells binds to this peptide in a competitive fashion and not to JNKK2, thereby allowing JNKK2 to promote JNK activation and the ensuing cell death. This cell death, i.e., apoptotic cell death is beneficial to reduce the growth of cancer cells.

Showing that Gadd45ß binds to and inhibits JNKK2 *in vitro*, thereby removing a barrier to apoptosis, coupled with the evidence that absence of Gadd 45ß *in vivo* removes a barrier to apoptosis, is sufficient to support the claim language which does **not** mention cancer, as the examiner admits. The claimed effect is that inactivation or absence of Gadd 45ß, *in vitro* or *in vivo*, increases JNK activation and consequently increases cell death. The examiner cannot reject terms that are not in the claims.

Regardless, just because so few cancer treatments have been successful, the Patent Office should be encouraging development of those early effects that show some promise—even if only *in vitro* and *in vivo* animal models, as shown here. Investigation on higher animals and eventually clinical trials, cannot proceed without funding. Funding at this level requires patent protection.

III. Claims Need Not Be Limited to Embodiments

Claims 1, 2, 6, and 36 are rejected Under 35 U.S.C. §112, 1st par.

It is well established that claims need not be limited to embodiments, as the examiner is requesting. To limit claims to the HIV-TAT-Peptide 1 fusion is unduly restrictive, giving no credence to the inventors' overall invention—modulation of JNKK2 by Gadd 45ß. Peptide 1 is an example to show that an agent can disrupt the Gadd45β-JNKK2 binding. The claims should not be limited to that embodiment, because the inventors of the present application have demonstrated for the first time, that preventing Gadd45β-JNKK2 interaction or binding results in an increased cell death.

> [00090] **cell permeable, fusion peptides** (such as TAT-fusion peptides) encompassing the amino acid regions of JNKK2 that come into direct contact with Gadd45β. These peptides will effectively compete with endogenous Gadd45β proteins for binding to JNKK2.

As the Federal Circuit stated eloquently:

> If everything in the specification were required to be read into the claims, or if structural claims were to be limited to devices operated precisely as a specification-described embodiment is operated, there would be no need for claims. Nor could an applicant, regardless of the prior art, claim more broadly than that embodiment. ... It is the claims that measure the invention. *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1326 (Fed. Cir. 2002).

Claims need not be limited to the preferred embodiment when the invention is more broadly described. *Inpro II Licensing, S.A.R.L. v. T-Mobile USA, Inc.*, 450 F.3d 1350, 1355 (Fed. Cir. 2006).

The Court has cautioned against limiting the claimed invention to preferred embodiments or specific examples in the specification. *Varco, L.P. v. Pason Sys. USA Corp.*, 436 F.3d 1368, 1375 (Fed. Cir. 2006).

IV. Claims 1 and 36 satisfy §112 second paragraph

Claims 1 and 36 have been rejected under 35 USC §112, 2nd par. Claim 36 relates to the cell-permeable peptide of claim 6, so the examiner's statement that "There is insufficient antecedent basis" (Office Action, page 5) is not understood. Claim 36 clearly states the amino acid sequences to be included in the peptides, so applicant cannot appreciate why one of skill could not understand the scope. The article modifying the sequence is amended to see if that helps.

Applicant disagrees there is no support for the term "interacts" in claim 1. The specification provides support for "interact" at least at the following instances (paragraph numbers refer to the published version of the application):

[0114] FIG. 19 shows physical interaction between Gadd45β and kinases in the JNK pathway, *in vivo*. ....., the ability of Gadd45β to physically interact with additional kinases in the JNK pathway was examined, focusing on those MAPKKKs, MAPKKs, and MAPKs that had been previously reported to be induced by TNF-Rs. ..... Notably, Gadd45β also interacted with JNKK2/MKK7, but not with the other JNK kinase, ... The interaction with JNKK2 might also explain the specificity of the inhibitory effects of Gadd45β on the JNK pathway.

[0115] FIG. 20 shows physical interaction between Gadd45.beta. and kinases in the JNK pathway, in vitro.....

[0116] FIG. 21 shows Gadd45β inhibits JNKK2 activity in vitro. Next, the functional consequences, in vitro, of the physical interactions of Gadd45β with kinases in the JNK pathway was assessed.....

[0117] FIGS. 22A-B shows Gadd45β inhibits JNKK2 activity in vivo. The ability of Gadd45β to inhibit JNKK2 was confirmed in vivo, in 3DO cells.....

[0120] FIGS. 23A-B shows that two distinct polypeptide regions in the kinase domain of JNKK2 are essential for the interaction with Gadd45β. By performing GST pull-down assays with GST- and GST-Gadd45β-coated beads, the regions of JNKK2 that are involved in the interaction with Gadd45.beta. were determined.....

[0122] The finding that Gadd45β directly contacts two distinct amino acid regions within the catalytic domain of JNKK2 provides mechanistic insights into the basis for the inhibitory effects of Gadd45β on JNKK2....

Example 12: JNKK2 (Also Known as MKK7)-Gadd45β Interacting Domains....

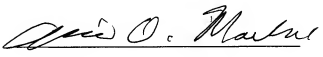
However, the term is replaced to relate how JNK is activated.

If pending claims are allowable, and a terminal disclaimer over U.S. Serial No. 10/263,330 is necessary, it will be filed.

Applicant requests the present amendment is entered for allowance or appeal. If there are still issues, an interview is also requested.

No other fees are believed due at this time, however, please charge any deficiencies or credit any overpayments to deposit account number 12-0913 with reference to our attorney docket number (21416-94575).

Respectfully submitted,



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